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Expression of apoptosis-related proteins and structural features of cell death in explanted aortocoronary saphenous vein bypass grafts

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This study aimed to investigate the features of cell death occurring in aortocoronary saphenous vein bypass grafts. Human aortocoronary saphenous vein bypass grafts with angiographic luminal stenosis of >75% were explanted from 14 patients at redo coronary artery bypass grafting. Proteins associated with apoptotic pathways were identified immunohistochemically using antibodies to Bcl-2, Fas, BAX, p53 and CPP32. Cells undergoing DNA fragmentation were identified by terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL). DNA synthesis was investigated using the antibody to proliferating cell nuclear antigen (PCNA). Ultrastructural features of cell death were examined by electron microscopy. Anti-apoptotic (Bcl-2) and pro-apoptotic (Bax, p53, CPP32 and Fas) proteins were expressed throughout the graft wall, but marked differences in the characteristics of cell death were noted between atherosclerotic and non-atherosclerotic areas of the intima. In atherosclerotic areas, pro-apoptotic proteins were widely expressed, but ultrastructural analysis failed to identify cells showing typical features of apoptosis. In these areas, necrotic cells were frequently observed, with negative correlation of Bcl-2 expression with TUNEL. Pro-apoptotic proteins showed no correlation with TUNEL. In contrast, in non-atherosclerotic areas of vein grafts, the expression of both anti-apoptotic (Bcl-2) and pro-apoptotic proteins (p53, Bax and CPP32) correlated with TUNEL. In atherosclerotic areas, non-atherosclerotic intimal areas, and in the underlying media, the numbers of TUNEL+ cells correlated with PCNA positivity. Ultrastructurally, apoptotic bodies and features of necrosis were observed in non-atherosclerotic areas of grafts. The present observations indicate that in atherosclerotic areas, cell death occurs mainly by necrosis, while in non-atherosclerotic areas, cell death occurs by both necrosis and apoptosis. An imbalance between DNA fragmentation and DNA synthesis may contribute to graft instability and failure.

Keywords: apoptosis, atherosclerosis, cell death, coronary artery disease, necrosis, saphenous vein bypass grafts

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